JAMA | Original Investigation

Discordance in Creatinine- and Cystatin C–Based eGFR and Clinical Outcomes
A Meta-Analysis

Michelle M. Estrella, MD, MHS; Shoshana H. Ballew, PhD; Yingying Sang, MSc; Morgan E. Grams, MD, PhD; Josef Coresh, MD, PhD; Aditya Surapaneni, PhD; Natalia Alencar de Pinho, PhD; Johan Ärnlöv, MD, PhD; Hermann Brenner, MD, MPH; Juan-Jesus Carrero, PharmD, PhD; Teresa K. Chen, MD, MHS; Debbie L. Cohen, MBBCH; Mary Cushman, MD, MSc; Ron T. Gansevoort, MD, PhD; Shih-Jen Hwang, PhD; Lesley A. Inker, MD, MS; Joachim H. Ix, MD, MAS; Keiko Kabasawa, MD, PhD, MPH; Tsuneo Konta, MD, PhD; Jennifer S. Lees, MBChB, PhD; Kevan R. Polkinghorne, MBChB, PhD; Michael G. Shlipak, MD, MPH; Robin W. M. Vernooij, MS; David C. Wheeler, MD; Ashok Kumar Yadav, PhD; Andrew S. Levey, MD; Kai-Uwe Eckardt, MD; for the Chronic Kidney Disease Prognosis Consortium Investigators and Collaborators

IMPORTANCE Estimated glomerular filtration rates (eGFRs) can differ according to whether creatinine or cystatin C is used for the eGFR calculation, but the prevalence and importance of these differences remain unclear.

OBJECTIVES To evaluate the prevalence of a discordance between cystatin C–based eGFR (eGFRcys) and creatinine-based eGFR (eGFRcr), identify characteristics associated with greater discordance, and evaluate associations of discordance with adverse outcomes.

DATA SOURCES Participants in the Chronic Kidney Disease Prognosis Consortium (CKD-PC).

STUDY SELECTION Participants with concurrent cystatin C and creatinine measurements and clinical outcome measurement.

DATA EXTRACTION AND SYNTHESIS Between April 2024 and August 2025, data were synthesized using individual-level meta-analysis.

MAIN OUTCOMES AND MEASURES The primary independent measurement was a large negative eGFR difference (eGFRdiff), defined as an eGFRcys that was at least 30% lower than eGFRcr. Secondary (dependent) outcomes included all-cause and cardiovascular mortality, atherosclerotic cardiovascular disease, heart failure, and kidney failure with replacement therapy.

RESULTS A total of 821 327 individuals from 23 outpatient cohorts (mean [SD] age, 59 [12] years; 48% female; 13.5% with diabetes; 40% with hypertension) and 39 639 individuals from 2 inpatient cohorts (mean [SD] age, 67 [16] years; 31% female; 30% with diabetes; 72% with hypertension) were included. Among outpatient participants, 11% had a large negative eGFRdiff (range, 3%-50%). Among inpatients, 35% had a large negative eGFRdiff. Among outpatient participants, at a mean (SD) follow-up of 11 (4) years, a large negative eGFRdiff, compared with an eGFRdiff between −30% and 30%, was associated with higher rates of all-cause mortality (28.4 vs 16.8 per 1000 person-years [PY]; hazard ratio [HR], 1.69 [95% CI, 1.57-1.82]), cardiovascular mortality (6.1 vs 3.8 per 1000 PY; HR, 1.61 [95% CI, 1.48-1.76]), atherosclerotic cardiovascular disease (13.3 vs 9.8 per 1000 PY; HR, 1.35 [95% CI, 1.27-1.44]), heart failure (13.2 vs 8.6 per 1000 PY; HR, 1.54 [95% CI, 1.40-1.68]), and kidney failure with replacement therapy (2.7 vs 2.1 per 1000 PY; HR, 1.29 [95% CI, 1.13-1.47]).

CONCLUSIONS AND RELEVANCE In the CKD-PC, 11% of outpatient participants and 35% of hospitalized patients had an eGFRcys that was at least 30% lower than their eGFRcr. In the outpatient setting, presence of eGFRcys at least 30% lower than eGFRcr was associated with significantly higher rates of all-cause mortality, cardiovascular events, and kidney failure.

JAMA. doi:10.1001/jama.2025.17578
Published online November 7, 2025.

Editorial
Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The Chronic Kidney Disease Prognosis Consortium Investigators and Collaborators appear in Supplement 2.

Corresponding Authors: Morgan E. Grams, MD, PhD (Morgan.Grams@nyulangone.org), and Josef Coresh, MD, PhD (ckdpc@nyulangone.org), New York University Grossman School of Medicine, 227 E 30th St, Room 707, New York, NY 10003.

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

SHOUT
SHARE
IT

Chronic kidney disease (CKD) diagnosis, staging, and treatment partially rely on estimated glomerular filtration rate (eGFR).[1] eGFR calculations typically use blood creatinine as the marker of glomerular filtration. However, creatinine levels can be affected by factors other than glomerular filtration rate (GFR) that can alter muscle metabolism, including diet, physical activity,[2] and medications, such as trimethoprim-sulfamethoxazole, which impair tubular creatinine secretion. Cystatin C is a filtration marker that is not affected by muscle metabolism or secreted by the kidney tubules. However, cystatin C may be affected by non-GFR factors, such as smoking, obesity, and inflammation.[2] Prior studies have reported that an eGFR calculated using both creatinine and cystatin C (eGFRcr-cys) better reflects measured GFR than eGFR based on creatinine alone (eGFRcr) and eGFR based on cystatin C alone (eGFRcys).[3,4] Substantial differences between eGFRcr and eGFRcys may exist in individual persons, and the presence of differences in eGFRcys and eGFRcr may have prognostic implications.[3,5-8] This study was designed to (1) characterize the prevalence of large eGFRcys and eGFRcr differences in the CKD Prognosis Consortium (CKD-PC), (2) identify characteristics associated with a discordant eGFRcys and eGFRcr, and (3) evaluate whether the presence of a discordant eGFRcys and eGFRcr is associated with higher rates of cardiovascular and kidney outcomes in the outpatient setting.

Key Points

Question Do individuals with a cystatin C–based estimated glomerular filtration rate (eGFRcys) value at least 30% lower than their creatinine-based estimated glomerular filtration rate (eGFRcr) have higher rates of mortality, cardiovascular events, and kidney failure compared with individuals whose eGFRcys is not at least 30% lower than their eGFRcr?

Findings In this individual participant–level meta-analysis of 821 327 participants from 23 cohorts, an eGFRcys at least 30% lower than eGFRcr was associated with higher mortality, cardiovascular events, and kidney failure with replacement therapy, compared with individuals whose eGFRcys was not at least 30% lower than their eGFRcr.

Meaning An eGFRcys value at least 30% lower than eGFRcr was associated with higher rates of mortality, cardiovascular events, and kidney failure with replacement therapy.

Methods

Participating Cohorts and Study Design

For this study, cohorts were eligible if their participants had creatinine and cystatin C measurements on the same day (eAppendix 1 in Supplement 1). Analyses were limited to participants 18 years or older with nonmissing age, sex, and same-day creatinine and cystatin C measurements. The institutional review board at New York University Grossman School of Medicine approved this study; informed consent for this secondary data analysis was waived due to the use of deidentified data. This study follows the PRISMA-Individual Participant Data reporting guidelines.

Kidney Measures

Creatinine was measured by each individual study with methods that used the IDMS (isotope dilution mass spectrometry); cystatin C was measured using methods standardized to International Federation of Clinical Chemistry and Laboratory Medicine standards. When measured in nonstandardized methods, values were statistically calibrated (eAppendix 1 in Supplement 1).[9,10]

eGFRcr and eGFRcr-cys were estimated using the 2021 CKD Epidemiology Collaboration (CKD-EPI) equations not including race[11] and eGFRcys using the 2012 CKD-EPI equation.[12] These equations are endorsed by the National Kidney Foundation and American Society of Nephrology Task Force,[13] adopted by most US clinical laboratories,[14] and recommended in the international clinical practice guidelines for CKD evaluation and management.[1]

Calculation of eGFR Differences

Primary analyses focused on large negative eGFR differences (eGFRdiffs), defined as an eGFRcys at least 30% lower than eGFRcr (ie, [(eGFRcys − eGFRcr)/eGFRcr] <−30%). A 30% difference has previously been used as a threshold for a meaningful difference in eGFR given the known biological and measurement variability in filtration markers.[1,11] Since clinical actions often rely on the KDIGO (Kidney Disease: Improving Global Outcomes) GFR (G) staging for CKD,[1] reclassification to a worse eGFR category using eGFRcys vs eGFRcr was also examined. Additional analyses included evaluating a large positive eGFRdiff (ie, [(eGFRcys − eGFRcr)/eGFRcr] >30%).

Covariate Definitions

Factors with known associations with eGFRdiff or that were likely to influence creatinine or cystatin C concentrations independent of GFR were evaluated as covariates,[15-17] including (1) sociodemographic and lifestyle factors (age, sex, and smoking status), (2) comorbidities (history of coronary heart disease, stroke, heart failure [HF], atrial fibrillation, peripheral artery disease [PAD], cancer, chronic obstructive pulmonary disease [COPD], and liver disease), and (3) clinical measures (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] and urine albumin-creatinine ratio [uACR]). uACR was natural log-transformed and missing uACR was analyzed as a separate binary category among clinical cohorts.

To combine data elements across cohorts, the CKD-PC Data Coordinating Center provided definitions to participating cohorts in the data request. eAppendix 1 in Supplement 1 details the ascertainment of each variable. In clinical datasets, comorbidity was defined at any time prior to the creatinine and cystatin C measurements by either the presence of 2 *International Classification of Diseases, Ninth Revision (ICD-9)* or *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)* diagnosis codes in the outpatient setting within 2 years of each other or the presence of 1 inpatient diagnosis code or problem list diagnosis. Investigators for each cohort were asked to specify if they used alternative variable definitions.

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Longitudinal Outcomes

All-cause mortality, cardiovascular mortality, atherosclerotic cardiovascular disease (ASCVD) events, incident HF, and kidney failure with replacement therapy (KFRT) were obtained from outpatient cohorts. eAppendix 1 in Supplement 1 details cohort-specific outcome definitions. Of the 22 cohorts with all-cause mortality data, 11 linked to national vital statistics registries, such as the National Death Index, and 9 cohorts used participant questionnaires, death certificates, or medical records. Of the 16 cohorts with cardiovascular mortality data, 9 identified events using diagnosis codes in medical records or death certificates and 7 used medical records, interviews of next of kin, and clinical adjudication. A total of 15 cohorts had ASCVD event data available, of which 7 used diagnosis codes and 8 used medical records with clinical adjudication. Of 13 cohorts with data available on HF, 7 used diagnosis codes and 6 used medical records with clinical adjudication. Twelve cohorts ascertained the outcome of KFRT. All US-based cohorts, SCREAM, and CKD-REIN identified KFRT events through linkage to national registries, such as the US Renal Data System,[18] while 3 cohorts ascertained KFRT events using medical record review. The UK Biobank used discharge diagnosis codes.

Statistical Analyses

Statistical analyses were conducted between April 2024 and August 2025. Analyses were performed among participating outpatient cohorts (a mix of clinical, research, and trial cohorts) and inpatient cohorts (clinical cohorts only) separately. To avoid confounding by reason for hospitalization, only outpatient cohorts were included in the evaluation of the association of eGFRcys and eGFRcr differences at baseline with longitudinal outcomes; the first visit for each individual with available concurrent creatinine and cystatin C was considered the baseline in each cohort.

Descriptive statistics of participant characteristics and kernel density plots of the distribution of eGFRdiff, weighted and unweighted by cohort sample size, were displayed within cohorts. The proportion of participants with a large negative eGFRdiff, by eGFRcr category, was summarized as the median (25th and 75th percentile) across outpatient cohorts and as the range between the 2 inpatient cohorts.

A logistic regression model was constructed to estimate the odds ratio (OR) and 95% CI of having a large negative eGFRdiff compared with an eGFRdiff of −30% to 30%. Within each cohort, if a variable was unavailable or missing in more than 50% of the participants, the variable was not included in the model; otherwise, missing values were imputed with the cohort mean value. The adjusted odds of a large negative eGFRdiff were estimated in each cohort using the meta-analyzed ORs and summarized as median (25th and 75th percentile) across outpatient cohorts and as the range between the 2 inpatient cohorts. A similar analysis was performed for the ORs associated with reclassification to a worse eGFR category. To provide hypothetical prevalences of a large eGFRdiff under different scenarios, we selected a baseline scenario of age 60 years, male, BMI of 30, eGFR of 45-59 mL/min/1.73 m^2, uACR of 10 mg/g, never smoked, and no comorbidities. We then varied the predicted prevalence by changing 1 risk factor at a time.

Within each outpatient cohort, Cox proportional hazards models were used to evaluate the association of eGFRdiff with long-term risks of adverse outcomes; random-effects models were used to meta-analyze hazard ratios (HRs). eGFRdiff was modeled both as a continuous (linear splines with knots at −30%, −15%, 0%, and 30%) and categorical variable (eg, large negative eGFRdiff, small eGFRdiff [reference], or positive eGFRdiff). Models adjusted for age; female sex; smoking status; history of hypertension, diabetes, coronary heart disease, stroke, HF, atrial fibrillation, PAD, cancer, COPD, or liver disease; BMI (continuous, with a spline knot at 30); eGFRcr category (≥90, 60-89, 45-59, 30-44, or <30 mL/min/1.73 m^2); and log-uACR (a missing indicator was also included for cohorts where uACR was missing in more than 10% of participants) (eAppendix 1 in Supplement 1). To demonstrate absolute risks of adverse outcomes, the ARIC study was used as the sample cohort for a baseline reflecting the overall outpatient mean characteristics in **Table 1**.[19-40]

For sensitivity analyses, cohorts were categorized based on their population composition (general, clinical, or CKD) and results were meta-analyzed across these cohort categories. Additional sensitivity analyses were performed in which data from the UK Biobank were excluded and in which models adjusted for eGFRcr-cys rather than eGFRcr.

Analyses were conducted using Stata/MP version 18 (StataCorp).

Results

Study Population

Of the 120 cohorts included in the CKD-PC, 23 were eligible for the current study. All 23 opted to participate and 2 had data for both the outpatient and inpatient cohorts. In the outpatient cohorts, the proportion of participants with creatinine measurements who also had cystatin C measurements ranged from 1.9% to 100% (Table 1). In the inpatient cohorts, the proportions of hospitalized patients with creatinine values who also had cystatin C measurements were 0.7% (of 1 283 836) and 6.6% (of 460 996), respectively, among VA and SCREAM participants. The 23 outpatient cohorts included 821 327 individuals, while the 2 inpatient cohorts included 39 639 individuals.

Among outpatient participants at baseline, the mean (SD) age was 59 (12) years, 48% were female, 13.5% had diabetes, and 40% had hypertension (Table 1). The overall mean (SD) eGFRcr and eGFRcys among outpatients were 87 (22) and 81 (25) mL/min/1.73 m^2, respectively (**Table 2**), with an overall median (IQI) eGFRdiff of −5.4% (−15.3% to 2.9%). Approximately 11.2% had a large negative eGFRdiff (eGFRcys at least 30% lower than eGFRcr); only 3.8% had a large positive eGFRdiff (eGFRcys at least 30% higher than eGFRcr). The eGFRdiff distribution varied across outpatient cohorts (**Figure 1**) (eFigure 1 in Supplement 1), with the proportion of participants with a large negative and positive eGFRdiff ranging from 2.8% to 49.8% and 0% to 27.9%, respectively. The overall mean (SD) eGFRcr-cys was 86 (23) (eTable 1 in Supplement 1).

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Table 1. Sociodemographic and Clinical Characteristics of Participants Overall and Within Each Cohort for the Outpatient and Inpatient Settings[a,b,c]

Cohort	Participants, No.	No. of participants with Cr and CysC (%)	Age, mean (SD), y	Female, %	Converted uACR, median (IQI), mg/g	Percentage of participants												
						Diabetes	Hypertension	BMI, mean (SD)	Formerly smoked	Currently smokes	CHD	Stroke	HF	Atrial fibrillation	PAD	Cancer	COPD	Liver disease
Outpatients	7 694 332	821 327 (11)	59 (12)	48	9 (6-18)	13.5	40	28 (5)	36	12	8.8	3.7	4.4	5.7	1.2	12	4.3	3.2
ICKD[19,d]	4079	930 (23)	49 (12)	33	160 (40-628)	36	95	25 (5)	13	15	4.3	NA	NA	NA	0.54	0.11	NA	0.11
CKD-REIN[20,d]	3814	3031 (79)	67 (13)	35	112 (22-516)	43	95	29 (6)	47	12	25	7.4	11	11	16.9	21	10	1.8
ULSAM[21,d]	1221	1103 (90)	71 (1)	0	8 (5-17)	13	77	26 (3)	NA	21	8.2	3.0	1.6	4.7	0.54	6.6	NA	1.3
VA	4 840 963	90 526 (1.9)	65 (14)	10	21 (7-99)	48	78	32 (7)	42	13	30	5.7	15	14	3.7	19	18	13
SCREAM[22,d]	2 257 866	151 502 (6.7)	62 (18)	48	12 (7-29)	18	59	NA	NA	NA	16	7.4	11	13	2.9	16	5.9	3.1
Takahata[23]	2551	1339 (52)	64 (10)	56	9 (6-17)	8.5	57	23 (3)	10	15	3.4	1.1	NA	NA	NA	NA	NA	NA
CRIB[24,d]	382	362 (95)	61 (14)	35	429 (89-1202)	18	94	27 (5)	50	13	19	7.5	NA	NA	NA	NA	NA	NA
MDRD[25,d]	1787	1044 (58)	52 (13)	39	114 (10-769)	9.6	74	27 (4)	NA	10	9.8	2.2	NA	NA	3.8	NA	NA	NA
ESTHER[26,d]	9835	9759 (99)	62 (7)	55	Dipstick	19	60	28 (5)	33	16	9.1	3.4	10	0.73	1.6	7.8	1.0	NA
REGARDS[27,d]	28 428	28 035 (99)	66 (9)	55	7 (5-16)	21	59	29 (10)	40	14	NA	6.2	NA	NA	NA	NA	NA	NA
GCKD[28,d]	5175	5175 (100)	61 (12)	40	51 (10-392)	36	96	30 (6)	73	26	20	8.3	19	21	7.5	12	6.9	4.5
Framingham[29]	2956	2596 (88)	59 (10)	54	6 (3-15)	8.8	39	28 (5)	NA	15	3.6	0.19	0.81	NA	NA	NA	NA	NA
CRIC[30,d]	5490	5485 (100)	60 (11)	44	46 (8-368)	51	87	32 (8)	42	13	NA	10	9.7	NA	NA	8.4	5.5	NA
NHANES[31,d]	10 396	4960 (48)	56 (21)	50	8 (5-18)	17	53	28 (6)	43	12	10	5.2	4.8	NA	NA	NA	NA	NA
ARIC[32,d]	11 529	11 303 (98)	63 (6)	56	4 (2-8)	17	48	29 (6)	44	15	8.6	2.3	5.7	1.9	3.5	NA	NA	NA
CHS[33,d]	4858	3377 (70)	78 (5)	60	10 (5-23)	17	50	27 (5)	44	7	24	6.2	9.3	NA	3.2	NA	NA	NA
MASTERPLAN[34,d]	678	477 (70)	60 (13)	31	120 (28-482)	23	NA	27 (4)	NA	17	20	7.3	NA	NA	NA	NA	NA	NA
PREVEND[35,d]	7940	7940 (100)	50 (13)	50	7 (5-13)	3.9	34	26 (4)	37	34	4.4	0.92	0.29	NA	NA	NA	NA	NA
UK Biobank[36]	469 124	467 963 (100)	57 (8)	54	9 (6-18)	4.7	27	27 (5)	35	10	3.9	1.6	0.062	1.5	0.26	8.7	1.0	NA
AASK[37,d]	1094	949 (87)	55 (11)	39	12 (5-130)	0	100	31 (7)	29	29	44	10	2.6	NA	3.4	NA	NA	NA
MESA[38,d]	6786	6770 (100)	62 (10)	53	5 (3-11)	13	45	28 (5)	37	13	0	0	0	0	0.059	8.6	NA	6.5
AusDiab[39,d]	11 237	10 558 (94)	52 (14)	55	5 (4-9)	6.4	32	27 (5)	29	16	6.6	2.5	NA	NA	NA	NA	NA	NA
Uonuma[40]	6143	6143 (100)	68 (10)	51	11 (6-25)	9.7	51	23 (3)	31	14	NA	0.42	NA	1.9	NA	9.4	0	NA
Inpatients	1 744 832	39 639 (0.2)	67 (16)	31	Range, 18-56	30	72	27 (7)	49	20	42	12	27	24	7.8	28	17	11
VA	1 283 836	9372 (0.7)	72 (12)	5.7	56 (12-321)	51	86	27 (7)	49	20	53	14	38	30	13	37	37	27
SCREAM[22,d]	460 996	30 267 (6.6)	65 (17)	39	18 (12-90)	24	68	NA	NA	NA	38	12	23	22	6.2	25	11	6.2

Abbreviations: BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CysC, cystatin C; HF, heart failure; PAD, peripheral artery disease; uACR, urine albumin-creatinine ratio.

[a] References refer to each cohort, but may not be the exact group of participants analyzed.

[b] Usable studies determined by number (proportion) of participants with concurrent CysC measurements among those with Cr measured.

[c] Cells with <11 participants do not include data linked to the US Renal Data System.

[d] All study names are expanded in eAppendix 2 in Supplement 1.

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.
Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Table 2. Distribution of Estimated Glomerular Filtration Rate (eGFR) and eGFR Difference (eGFRdiff) in the Outpatient and Inpatient Settings, Overall and by Cohort[a,b]

Cohort	Study participants, No.	eGFRcr, mean (SD), mL/min/1.73 m^2	eGFRcys, mean (SD), mL/min/1.73 m^2	(eGFRcys − eGFRcr)/ eGFRcr, median (IQR), %	(eGFRcys − eGFRcr)/ eGFRcr <−30% (%)	(eGFRcys − eGFRcr)/ eGFRcr >30% (%)
Outpatients, overall	821 327	87 (22)	81 (25)	−5.4 (−15.3 to 2.9)	92 154 (11.2)	31 024 (3.8)
ICKD[c]	930	47 (17)	40 (31)	−29.7 (−52.2 to 10.2)	463 (49.8)	151 (16.2)
CKD-REIN[c]	3031	36 (14)	27 (11)	−26.3 (−36.7 to −15.2)	997 (41.4)	17 (0.7)
ULSAM[c]	1103	81 (11)	62 (13)	−23.5 (−31.4 to −13.9)	328 (29.7)	3 (0.3)
VA[c]	90 526	67 (25)	58 (27)	−16.9 (−32.1 to 2.4)	25 641 (28.4)	7781 (8.6)
SCREAM[c]	151 502	80 (26)	73 (31)	−9.8 (−27.5 to 6.0)	35 102 (21.9)	7857 (5.2)
Takahata	1339	101 (11)	82 (18)	−17.6 (−28.1 to −8.6)	279 (20.8)	0
CRIB[c]	362	23 (12)	21 (12)	−6.6 (−23.7 to 12.0)	57 (15.7)	42 (11.6)
MDRD[c]	1044	36 (16)	32 (14)	−10.7 (−23.6 to 4.1)	158 (15.1)	56 (5.4)
ESTHER[c]	9759	87 (20)	80 (16)	−9.9 (−21.9 to 4.8)	1175 (12.0)	1026 (10.5)
REGARDS[c]	28 035	84 (19)	78 (23)	−6.7 (−20.3 to 5.4)	3178 (11.5)	1104 (3.9)
GCKD[c]	5175	52 (19)	50 (20)	−5.1 (−19.0 to 9.8)	544 (10.6)	376 (7.3)
Framingham	2596	92 (17)	85 (18)	−7.7 (−18.1 to 2.4)	217 (8.4)	81 (3.1)
CRIC[c]	5485	48 (16)	54 (23)	10.5 (−9.3 to 32.9)	427 (7.8)	1528 (27.9)
NHANES[c]	4960	87 (25)	88 (30)	1.2 (−12.4 to 14.0)	365 (7.4)	533 (10.7)
ARIC[c]	11 303	88 (16)	84 (19)	−3.3 (−15.0 to 7.0)	732 (6.5)	565 (5.0)
CHS[c]	3377	69 (16)	66 (18)	−5.0 (−16.6 to 7.1)	207 (6.1)	174 (5.2)
MASTERPLAN[c]	477	38 (16)	40 (19)	3.2 (−11.9 to 21.0)	27 (5.7)	87 (18.2)
PREVEND[c]	7940	100 (15)	93 (19)	−6.2 (−16.7 to 2.7)	441 (5.6)	103 (1.3)
UK Biobank	467 963	95 (13)	89 (16)	−5.4 (−15.3 to 2.9)	20 845 (4.5)	8652 (1.8)
AASK[c]	949	42 (13)	45 (18)	4.8 (−10.9 to 22.8)	43 (4.5)	167 (17.6)
MESA[c]	6770	90 (16)	89 (20)	−0.2 (−11.7 to 9.6)	298 (4.4)	364 (5.4)
AusDiab[c]	10 558	99 (17)	100 (23)	2.6 (−7.3 to 11.0)	460 (4.4)	343 (3.2)
Uonuma	6143	95 (12)	92 (18)	−1.6 (−10.2 to 4.2)	170 (2.8)	14 (0.2)
Inpatients, overall	39 639	69 (32)	57 (33)	−29.1 to −15.4	13 513 (34.2)	2556 (6.4)
VA	9372	58 (32)	41 (26)	−29.1 (−46.0 to −8.3)	4548 (48.8)	648 (7.0)
SCREAM[c]	30 267	73 (32)	62 (34)	−15.4 (−33.7 to 2.8)	8965 (29.6)	1908 (6.3)

Abbreviations: eGFRcr, creatinine-based eGFR; eGFRcys, cystatin C–based eGFR.

[a] Table presents data only from participants included in the analyses. eGFRdiff percentage reflects the median cohort and 25th and 75th percentile cohort for outpatients and the range of the 2 cohorts for inpatients.

[b] Any cells with fewer than 11 participants do not include data linked to the US Renal Data System.

[c] All study names are expanded in eAppendix 2 in Supplement 1.

For the inpatient cohorts, the mean (SD) age was 67 (16) years, 31% were female, 30% had diabetes, and 72% had hypertension (Table 1). Among hospitalized participants, mean (SD) eGFRcr was 69 (32) and mean eGFRcys was 57 (33) mL/min/1.73 m^2 (Table 2), with a median (IQI) eGFRdiff of −15.4% (−33.7% to 2.8%) and −29.1% (−46.0% to −8.3%), respectively, in the SCREAM and VA cohorts. Approximately 35% of inpatients had a large negative eGFRdiff and 14.5% had a large positive eGFRdiff. The mean (SD) eGFRcr-cys was 63 (33) (eTable 1 in Supplement 1).

Percentage of Participants With a Large Negative eGFRdiff by eGFRcr Category

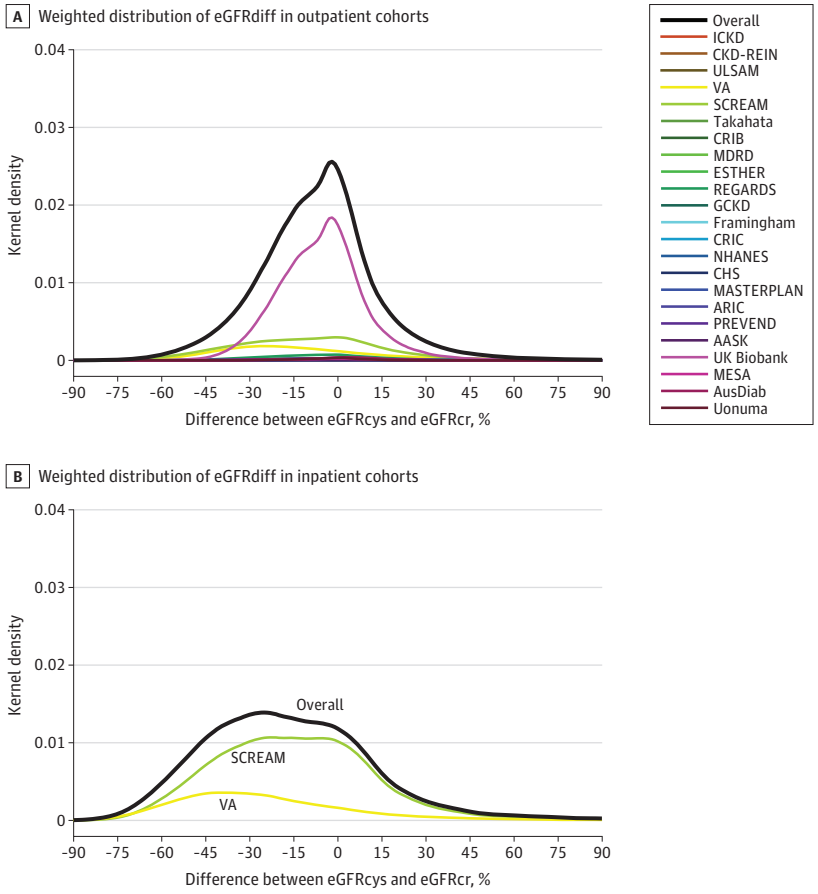
Table 3 shows the percentage of individuals who had a large negative eGFRdiff within each eGFRcr category, summarized across cohorts. Among outpatient cohorts, the median percentage of individuals with a large negative eGFRdiff was generally greater at lower eGFRcr values. For example, within the eGFRcr categories of ≥90 and 60-89 mL/min/1.73 m^2, the median percentages were both 7.8%. However, median values were 12.3%, 17.6%, and 14.8% within the 45-59, 30-44, and <30 mL/min/1.73 m^2 categories, respectively. Compared with the outpatient setting, the proportions of individuals with a large negative eGFRdiff for each eGFR category were higher within inpatient cohorts (Table 3), ranging from 22.5% to 57.2%, 41.1% to 57.0%, and 23.8% to 24.4% among those with an eGFRcr of ≥90, 45-59, and <30 mL/min/1.73 m^2, respectively.

The percentage of patients reclassified to a lower eGFR category was higher in the inpatient than in the outpatient setting (Table 3). For instance, among those with an eGFRcr of 45-59 mL/min/1.73 m^2, the median percentage reclassified was 34.0% in the outpatient setting compared with a range of 63.9% to 75.9% in the inpatient setting. Percent values that compared eGFRcr-cys with eGFRcr followed a similar pattern, with greater prevalence of reclassification in the inpatient compared with outpatient setting (eTable 2 in Supplement 1). For example, among those with an eGFRcr

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Figure 1. Weighted Distribution of the Estimated Glomerular Filtration Rate Difference (eGFRdiff) Across Each Cohort



eGFRdiff was calculated as (eGFRcys − eGFRcr)/eGFRcr. The overall line has a weight of 1. All individual cohort lines have weights according to the proportion of their sample n to the overall N. All study names are expanded in eAppendix 2 in Supplement 1.

eGFRcr indicates creatinine-based estimated glomerular filtration rate; eGFRcys, cystatin C–based estimated glomerular filtration rate.

of 45-59 mL/min/1.73 m^2, the median percentage reclassified was 17.8% in the outpatient cohorts but ranged from 41.2% to 57% in the inpatient cohorts.

Characteristics Associated With eGFRdiff

Characteristics associated with a large negative eGFRdiff included current smoking (pooled prevalence of 21.0% among individuals with a large negative eGFRdiff vs 11.0% among those with an eGFRdiff of −30% to 30%; meta-analyzed adjusted OR, 2.09 [95% CI, 1.59-2.74]), HF (18.5% vs 2.6%; OR, 1.81 [95% CI, 1.53-2.14]), and liver disease (9.7% vs 5.7%; OR, 1.79 [95% CI, 1.12-2.88]). Older age (pooled mean [SD] age, 69 [13] vs 58 [12] years; OR, 1.68 per 10 years older [95% CI, 1.55-1.81]), COPD (15.4% vs 2.9%; OR, 1.61 [95% CI, 1.38-1.89]), PAD (4.5% vs 0.8%; OR, 1.60 [95% CI, 1.48-1.74]), and BMI (pooled mean [SD] BMI, 31 [8] vs 28 [6]; OR, 1.53 per 5 units higher [95% CI, 1.37-1.69]) also had statistically significant associations with a large negative eGFRdiff (**Table 4**). Compared with an eGFRcr of 45-59 mL/min/1.73 m^2, an eGFRcr ≥90 mL/min/1.73 m^2 was associated with 1.56-fold (95% CI, 1.15-2.10) higher meta-analyzed adjusted odds (pooled prevalence of 37.2% among individuals with a large negative eGFRdiff vs 60.3% among those with an eGFRdiff of −30% to 30%), while an eGFRcr <30 mL/min/1.73 m^2 was associated with 0.56-fold (95% CI, 0.46-0.69) lower odds (4.1% vs 1.6%) of a large negative eGFRdiff. eGFRcr of 90 mL/min/1.73 m^2 (pooled prevalence of 63.0% among individuals reclassified to a worse eGFR category vs 59.9% among those who stayed in the same eGFR category; OR, 3.35 vs eGFRcr of 45 mL/min/1.73 m^2 [95% CI, 2.55-4.40]), older age (pooled mean [SD] age of 66 [12] vs 58 [12] years; OR, 2.01 per 10 years older [95% CI, 1.75-2.31]), and current smoking (17.7% vs 11.1%; OR, 1.97 [95% CI, 1.72-2.27]) were some of the characteristics associated with the meta-analyzed adjusted odds of downward eGFR staging when using eGFRcr-cys (eTable 3 in Supplement 1).

In the inpatient setting, the estimated prevalence of a large negative eGFRdiff was 38.1% and 43.8% in the 2 cohorts. Characteristics associated with higher likelihood of a large negative eGFRdiff, compared with an eGFRdiff between −30% and 30%, among hospitalized patients included HF (pooled prevalence of 38.0% among individuals with a large negative eGFRdiff vs 21.1% among those with an eGFRdiff of −30% to 30%; OR, 1.63 [95% CI, 1.21-2.19]) and liver disease (15.8% vs 8.5%; OR, 1.74 [95% CI, 1.25-2.41]) (Table 4); older age, diabetes, PAD, and COPD were also associated with a higher likelihood of a large negative eGFRdiff. eGFR categories less than 45 mL/min/1.73 m^2 were associated with lower odds of a large negative eGFRdiff vs an eGFR of 45 to 59 mL/min/1.73 m^2

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Table 3. Observed Percentage of Individuals Who Had a Large Negative Estimated Glomerular Filtration Rate Difference (eGFRdiff) or Were Reclassified to a Worse Category With Cystatin C–Based eGFR (eGFRcys) Relative to Creatinine-Based eGFR (eGFRcr), by eGFRcr Category

	eGFRcr category, mL/min/1.73 m^2				
	≥90	60-89	45-59	30-44	<30
Outpatient, median percentage across cohorts (25th to 75th percentile)[a]					
No.	455 258	260 629	52 426	33 209	16 556
(eGFRcys − eGFRcr)/eGFRcr <−30%	7.8 (4.0-17.9)	7.8 (5.8-23.3)	12.3 (7.1-27.0)	17.6 (6.2-29.4)	14.8 (9.2-31.9)
Reclassified to a worse eGFR category with eGFRcys relative to eGFRcr	45.2 (29.0-63.3)	16.1 (12.7-36.2)	34.0 (22.4-58.5)	28.3 (18.8-41.7)	NA
Inpatient, percentage in 2 cohorts					
No.	13 055	10 972	4840	4652	6120
SCREAM[b]: (eGFRcys − eGFRcr)/eGFRcr <−30%	22.5	32.1	41.1	41.1	24.4
SCREAM[b]: reclassified to a worse eGFR category with eGFRcys relative to eGFRcr	45.3	46.2	63.9	56.5	NA
VA[b]: (eGFRcys − eGFRcr)/eGFRcr <−30%	57.2	63.0	57.0	49.5	23.8
VA[b]: reclassified to a worse eGFR category with eGFRcys relative to eGFRcr	79.0	75.9	75.9	65.2	NA

Abbreviation: NA, not applicable.

[a] The median (25th to 75th percentile) was the raw percentage summarized across cohorts (chronic kidney disease cohorts were excluded from eGFRcr ≥90 and 60-89 due to small sample size).

[b] All study names are expanded in eAppendix 2 in Supplement 1.

(eGFR 30-44: 15.1% vs 9.7%; OR, 0.79 [95% CI, 0.64-0.98] vs eGFR <30: 11.0% vs 14.4%; OR, 0.33 [95% CI, 0.17-0.64]).

eGFRdiff and Mortality in the Outpatient Cohorts

In the outpatient cohorts, during a mean (SD) follow-up of 11 (4) years, 107 584 all-cause deaths and 25 465 cardiovascular deaths occurred. Additionally, 35 133 ASCVD events, 34 017 HF events, and 10 060 KFRT events occurred (eTable 4 in Supplement 1). **Figure 2** shows the HR for each outcome across the range of eGFRdiffs; larger negative eGFRdiff values were associated with greater risk for every adverse outcome listed below.

Among outpatients, compared with an eGFRdiff of −30% to 30%, a large negative eGFRdiff was associated with higher risk for all-cause mortality (28.4 vs 16.8 per 1000 person-years [PY]; HR, 1.69 [95% CI, 1.57-1.82]), cardiovascular mortality (6.1 vs 3.8 per 1000 PY; HR, 1.61 [95% CI, 1.48-1.76]), ASCVD (13.3 vs 9.8 per 1000 PY; HR, 1.35 [95% CI, 1.27-1.44]), HF (13.2 vs 8.6 per 1000 PY; HR, 1.54 [95% CI, 1.40-1.68]), and KFRT (2.7 vs 2.1 per 1000 PY; HR, 1.29 [95% CI, 1.13-1.47]) (**Table 5**). Participants with a large positive eGFRdiff had lower risks compared with participants with an eGFRdiff between −30% and 30% for all-cause mortality (12.9 vs 16.8 per 1000 PY; HR, 0.76 [95% CI, 0.73-0.80]), cardiovascular mortality (3.0 vs 3.8 per 1000 PY; HR, 0.79 [95% CI, 0.67-0.91]), ASCVD (8.0 vs 9.8 per 1000 PY; HR, 0.81 [95% CI, 0.74-0.89]), HF (6.5 vs 8.6 per 1000 PY; HR, 0.76 [95% CI, 0.69-0.84]), and KFRT (2.1 vs 2.1 per 1000 PY; HR, 1.04 [95% CI, 0.84-1.29]).

For individuals with a large negative eGFRdiff compared with those with an eGFRdiff between −30% and 30%, when the associations of a large negative eGFRdiff with outcomes were adjusted for eGFRcr-cys instead of eGFRcr, risk estimates were attenuated: all-cause mortality (24.9 vs 16.8 per 1000 PY; HR, 1.48 [95% CI, 1.37-1.59]), cardiovascular mortality (5.2 vs 3.8 per 1000 PY; HR, 1.38 [95% CI, 1.26-1.52]), ASCVD (11.9 vs 9.8 per 1000 PY; HR, 1.21 [95% CI, 1.15-1.28]), and HF (11.3 vs 8.6 per 1000 PY; HR, 1.32 [95% CI, 1.21-1.45]), respectively. In contrast, the risk estimate for KFRT reversed direction, with a large negative eGFRdiff associated with lower risk (1.5 vs 2.1 per 1000 PY; HR, 0.73 [95% CI, 0.64-0.84]) (Table 5). eFigure 2 in Supplement 1 demonstrates the associations between eGFRdiff and outcomes across cohort types.

Risk estimates were similar when UK Biobank data were excluded (eTable 5 in Supplement 1). In these analyses, a large negative eGFRdiff, compared with an eGFRdiff between −30% and 30%, was associated with higher risk for all-cause mortality (28.2 vs 16.8 per 1000 PY; HR, 1.67 [95% CI, 1.53-1.83]), cardiovascular mortality (5.9 vs 3.8 per 1000 PY; HR, 1.57 [95% CI, 1.41-1.74]), ASCVD (13.1 vs 9.8 per 1000 PY; HR, 1.33 [95% CI, 1.26-1.41]), HF (12.9 vs 8.6 per 1000 PY; HR, 1.50 [95% CI, 1.35-1.67]), and KFRT (2.7 vs 2.1 per 1000 PY; HR, 1.30 [95% CI, 1.12-1.50]) compared with an eGFRdiff of −30% to 30%.

Discussion

Among 821 327 outpatient participants in the CKD-PC, 11% had a large negative eGFRdiff. Among 39 639 hospitalized patients in the CKD-PC, 35% had a large negative eGFRdiff. The difference between eGFRcr and eGFRcys was greater and the prevalence of a large negative eGFR higher among inpatient cohorts compared with outpatient cohorts. Characteristics associated with a large negative eGFRdiff included older age,

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Table 4. Characteristics of Participants and Adjusted Odds Ratios (ORs) According to a Difference Between Cystatin C–Based Estimated Glomerular Filtration Rate (eGFRcys) and Creatinine-Based eGFR (eGFRcr) of Less Than −30% Compared With a Difference Between −30% and 30%, in the Outpatient and Inpatient Settings[a]

Characteristic	Outpatient			Inpatient		
	eGFRdiff <−30% (n = 92 154), No. (%)	eGFRdiff −30% to 30% (n = 698 149), No. (%)	Adjusted OR (95% CI)	eGFRdiff <−30% (n = 13 513), No. (%)	eGFRdiff −30% to 30% (n = 23 570), No. (%)	Adjusted OR (95% CI)
Age, mean (SD), per 10 y older, y	69 (13)	58 (12)	1.68 (1.55-1.81)	72 (14)	64 (16)	1.27 (1.21-1.33)
≤40	2020 (2.2)	26 641 (3.8)		585 (4.3)	2315 (9.8)	
41-60	17 167 (18.6)	331 639 (47.5)		1561 (11.6)	5479 (23.2)	
61-80	52 531 (57.0)	316 702 (45.4)		7327 (54.2)	12 220 (51.8)	
≥81	20 436 (22.2)	23 167 (3.3)		4040 (29.9)	3555 (15.1)	
Sex						
Female	36 495 (39.6)	344 469 (49.3)	1.17 (1.10-1.24)	4137 (30.6)	7483 (31.7)	1.07 (0.80-1.43)
Male	55 659 (60.4)	353 680 (50.7)	1 [Reference]	9376 (69.4)	16 087 (68.3)	1 [Reference]
Hypertension	63 012 (68.6)	254 282 (36.4)	1.12 (1.02-1.22)	10 963 (81.1)	15 977 (67.8)	1.04 (0.97-1.11)
Diabetes	29 642 (32.2)	76 546 (11.0)	1.15 (1.08-1.23)	5045 (37.3)	6268 (26.6)	1.18 (1.12-1.25)
Never smoked	22 808 (40.4)	309 202 (52.9)	1 [Reference]	1262 (28.5)	1303 (32.2)	1 [Reference]
Formerly smoked	21 587 (38.2)	208 870 (35.7)	1.03 (0.95-1.11)	2298 (51.9)	1914 (47.3)	1.21 (1.09-1.34)
Currently smokes	11 854 (21.0)	64 299 (11.0)	2.09 (1.59-2.74)	872 (19.7)	828 (20.5)	1.04 (0.91-1.19)
Coronary heart disease	20 323 (23.1)	46 315 (7.0)	1.20 (1.11-1.30)	6071 (44.9)	9732 (41.3)	0.78 (0.60-0.99)
Stroke	9260 (10.1)	19 735 (2.8)	1.23 (1.07-1.42)	2102 (15.6)	2498 (10.6)	1.13 (0.88-1.46)
Heart failure	16 188 (18.5)	16 899 (2.6)	1.81 (1.53-2.14)	5134 (38.0)	4968 (21.1)	1.63 (1.21-2.19)
Atrial fibrillation	15 998 (18.9)	25 068 (4.0)	1.20 (1.09-1.33)	4275 (31.6)	4811 (20.4)	1.09 (0.95-1.26)
Peripheral artery disease	3866 (4.5)	5166 (0.8)	1.60 (1.48-1.74)	1528 (11.3)	1427 (6.1)	1.38 (1.12-1.69)
Cancer	18 358 (21.4)	66 371 (10.5)	1.14 (1.01-1.29)	4674 (34.6)	5848 (24.8)	1.25 (1.03-1.51)
Chronic obstructive pulmonary disease	12 990 (15.4)	17 784 (2.9)	1.61 (1.38-1.89)	3505 (25.9)	3125 (13.3)	1.36 (1.24-1.50)
Liver disease	6170 (9.7)	10 249 (5.7)	1.79 (1.12-2.88)	2139 (15.8)	2006 (8.5)	1.74 (1.25-2.41)
BMI <30, per 5 units higher			1.06 (0.89-1.27)			0.98 (0.92-1.04)
BMI ≥30, per 5 units higher			1.53 (1.37-1.69)			1.20 (1.12-1.28)
Continuous BMI, mean (SD)	31 (8)	28 (6)		26 (8)	26 (7)	
<25	11 583 (20.7)	187 799 (32.1)		2225 (49.2)	1904 (45.9)	
25-29	16 061 (28.6)	239 076 (40.9)		1128 (24.9)	1113 (26.9)	
30-35	12 643 (22.5)	105 489 (18.0)		635 (14.0)	644 (15.6)	
>35	15 798 (28.2)	52 296 (8.9)		536 (11.8)	482 (11.6)	
eGFRcr, mean (SD), mL/min/1.73 m^2	76 (25)	90 (20)		68 (29)	73 (33)	
≥90	34 241 (37.2)	420 759 (60.3)	1.56 (1.15-2.10)	3638 (26.9)	9262 (39.3)	0.92 (0.55-1.52)
60-89	31 398 (34.1)	212 703 (30.5)	1.23 (1.06-1.44)	4147 (30.7)	6245 (26.5)	1.08 (0.67-1.74)
45-59	12 959 (14.1)	33 065 (4.7)	1 [Reference]	2204 (16.3)	2379 (10.1)	1 [Reference]
30-44	9822 (10.7)	20 698 (3.0)	0.89 (0.78-1.01)	2044 (15.1)	2281 (9.7)	0.79 (0.64-0.98)
<30	3734 (4.1)	10 924 (1.6)	0.56 (0.46-0.69)	1480 (11.0)	3403 (14.4)	0.33 (0.17-0.64)
lnACR, median (IQR), per e-fold higher	17 (11-68)	9 (6-18)	1.17 (1.14-1.20)	25 (12-99)	12 (12-69)	1.06 (0.99-1.13)
<30	27 568 (59.5)	232 244 (80.2)		2127 (47.9)	3521 (54.8)	
30-300	12 825 (27.7)	44 197 (15.3)		1451 (32.7)	1619 (25.2)	
>300	5964 (12.9)	13 296 (4.6)		858 (19.3)	1282 (20.0)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); eGFRdiff, estimated glomerular filtration rate difference; lnACR, natural log of albumin to creatinine ratio.

[a] Some cells are blank because ORs are included only for continuous variables.

current smoking, HF, liver disease, COPD, PAD, and higher BMI and were similar between the outpatient and inpatient settings. Individuals with a large negative eGFRdiff had higher risks for all-cause and cardiovascular mortality, ASCVD, HF, and KFRT, compared with those without a large difference between eGFRcr and eGFRcys. Therefore, a large proportion of individuals had an eGFRcys that was at least 30% lower than the eGFRcr and those in the outpatient setting with this difference had higher rates of adverse outcomes, compared with those with an eGFRdiff of less than −30%.

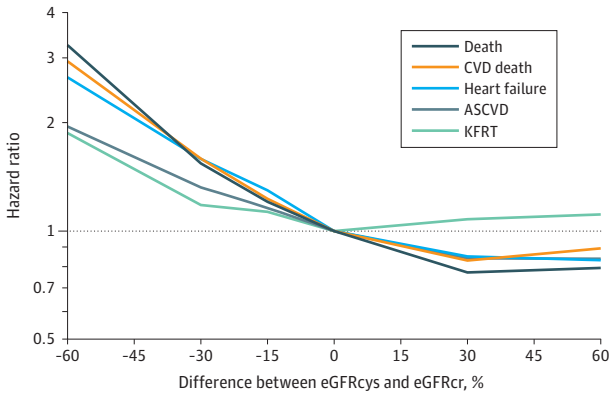
© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Most prior studies of eGFRdiff evaluated outpatient populations only and used only single cohorts for analyses.[5-8,41] For example, the prevalence of a large negative eGFRdiff was 8% in a CKD cohort[5] and 16% in an older population.[41] To the study investigators' knowledge, only 1 prior study included hospitalized patients, which reported a median eGFRdiff of −18 mL/min/1.73 m^2 in 684 hospitalized patients vs 4 mL/min/1.73 m^2 in 1367 outpatients.[42] The present analysis builds upon prior work because it consists of a comprehensive analysis of participant-level data from 23 outpatient cohorts and evaluation of 2 large inpatient cohorts. Consistent with prior literature,[5,41] the proportion of individuals with a large negative eGFRdiff varied across the CKD-PC cohorts, ranging from 3% to 50%, and were higher in the inpatient vs outpatient settings. Differences in the proportion of participants with clinical characteristics associated with greater eGFRdiff may explain the variable prevalence of a large negative eGFRdiff across studies and between inpatient and outpatient settings.

Prior studies reported that persons with a large negative eGFRdiff have higher risk of all-cause mortality,[5,8] ASCVD,[8,43] incident HF,[6,8] and KFRT.[8] Findings from the present study are consistent with these observations. The primary analysis in this report adjusted for eGFRcr, the current standard of care. When associations of eGFRdiff with longitudinal outcomes were adjusted for eGFRcr-cys (the most accurate estimate of measured GFR in most settings) rather than eGFRcr, the risk estimates were attenuated for all-cause mortality and cardiovascular outcomes and reversed for KFRT. The attenuation is likely due to the stronger association of cystatin C compared with creatinine with mortality and cardiovascular events, demonstrated consistently across prior epidemiological studies.[44-46] In contrast, the reversal of the risk estimate for KFRT upon adjustment for eGFRcr-cys may be explained by usual clinical practice wherein dialysis initiation is largely determined by eGFRcr; therefore, adjustment for eGFRcr-cys

Figure 2. Association of the Estimated Glomerular Filtration Rate Difference (eGFRdiff) With Risks of Long-Term Adverse Outcomes in the Outpatient Cohorts



eGFRdiff was calculated as (eGFRcys − eGFRcr)/eGFRcr and modeled as a linear spline with knots at −30%, −15%, 0%, and 30%. Models adjusted for age, sex, hypertension, diabetes, former and current smoking, history of coronary heart disease, stroke, heart failure, atrial fibrillation, peripheral artery disease, cancer, liver disease, chronic obstructive pulmonary disease, body mass index (linear splines with knot at 30), eGFRcr categories (≥90, 60-89, 45-59, 30-44, <30 mL/min/1.73 m^2), albumin to creatinine ratio missing indicator, and log-urine albumin to creatinine ratio. Linear splines were also used for eGFRdiff.

ASCVD indicates atherosclerotic cardiovascular disease; CVD, cardiovascular disease; eGFRcr, creatinine-based estimated glomerular filtration rate; eGFRcys, cystatin C–based estimated glomerular filtration rate; KFRT, kidney failure with replacement therapy.

Table 5. Associations of Large Negative and Positive Estimated Glomerular Filtration Rate Differences (eGFRdiffs) Between Cystatin C–Based eGFR (eGFRcys) and Creatinine-Based eGFR (eGFRcr) With Risks of Long-Term Adverse Outcomes in All Outpatient Cohorts Adjusted for eGFRcr and eGFRcr-cys Instead of eGFRcr[a]

	eGFRdiff <−30%[b]		eGFRdiff −30% to 30%[b]		eGFRdiff >30%[b]	
	HR (95% CI)	IR, 1000 PY	HR (95% CI)	IR, 1000 PY	HR (95% CI)	IR, 1000 PY
Analyses in all outpatient cohorts adjusted for eGFRcr						
All-cause mortality	1.69 (1.57-1.82)	28.4	1 [Reference]	16.8	0.76 (0.73-0.80)	12.9
CVD mortality	1.61 (1.48-1.76)	6.1	1 [Reference]	3.8	0.79 (0.67-0.91)	3.0
ASCVD	1.35 (1.27-1.44)	13.3	1 [Reference]	9.8	0.81 (0.74-0.89)	8.0
Heart failure	1.54 (1.40-1.68)	13.2	1 [Reference]	8.6	0.76 (0.69-0.84)	6.5
KFRT	1.29 (1.13-1.47)	2.7	1 [Reference]	2.1	1.04 (0.84-1.29)	2.1
Sensitivity analyses with adjustment for eGFRcr-cys instead of eGFRcr						
All-cause mortality	1.48 (1.37-1.59)	24.9	1 [Reference]	16.8	0.86 (0.79-0.93)	14.5
CVD mortality	1.38 (1.26-1.52)	5.2	1 [Reference]	3.8	0.87 (0.76-1.00)	3.3
ASCVD	1.21 (1.15-1.28)	11.9	1 [Reference]	9.8	0.88 (0.81-0.96)	8.6
Heart failure	1.32 (1.21-1.45)	11.3	1 [Reference]	8.6	0.86 (0.78-0.96)	7.4
KFRT	0.73 (0.64-0.84)	1.5	1 [Reference]	2.1	1.63 (1.34-1.99)	3.4

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; HR, hazard ratio; IR, incidence rate; KFRT, kidney failure with replacement therapy; PY, person-years.

[a] Models adjusted for age, sex, hypertension, diabetes, former and current smoking, history of coronary heart disease, stroke, heart failure, atrial fibrillation, peripheral artery disease, cancer, liver disease, chronic obstructive pulmonary disease, body mass index (linear splines with knot at 30), eGFRcr categories (≥90, 60-89, 45-59, 30-44, and <30 mL/min/1.73 m^2), albumin to creatinine ratio missing indicator, and log-urine albumin to creatinine ratio. To demonstrate absolute risks of adverse outcomes, the ARIC study was used as the sample cohort for a baseline reflecting the overall outpatient mean characteristics in Table 1.

[b] eGFRdiff was calculated as (eGFRcys − eGFRcr)/eGFRcr.

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

becomes an artificial construct, with eGFRdiff serving as a proxy of eGFRcr in the model.

This study has potential clinical implications. First, results from this study suggest that cystatin C testing identifies a large number of individuals who may have worse GFR than would be suggested by eGFRcr alone. These individuals may benefit from a more precise estimate of GFR for clinical decision-making. Data support the use of eGFRcr-cys as the most accurate estimate of GFR in the outpatient setting[11]; however, evidence determining which eGFR estimating equation is most accurate among hospitalized patients remains unclear. The large percentage of hospitalized patients with a large negative eGFRdiff underscores the need for additional studies that directly measure GFR in the inpatient setting. Second, the findings suggest that cystatin C testing among older individuals; those with comorbid conditions, such as HF or liver disease; and hospitalized patients may be particularly useful. Third, the eGFRdiff provides prognostic information on important clinical outcomes and supports laboratory reporting of eGFRcys and eGFRcr-cys alongside eGFRcr, as large differences may identify outpatients at higher risk of adverse long-term outcomes.

Limitations

This study has limitations. First, other GFR estimating equations, such as the European Kidney Function Consortium equation, were not evaluated. Second, differences in measurement methods for creatinine or cystatin C across cohorts could explain some variation among cohorts. Third, study designs and outcome measurements differed across cohorts, and outcomes were largely based on diagnosis codes. Fourth, among hospitalized patients, there may have been selection bias regarding who underwent cystatin C testing. Fifth, data were unavailable for potential confounders, such as muscle mass or thyroid disorders, or factors unique to the inpatient setting that may affect creatinine or cystatin C levels. Sixth, the UK Biobank comprised approximately half of the outpatient study population and was predominantly White (>90%); however, sensitivity analyses that excluded data from the UK Biobank yielded associations of large eGFRdiffs with outcomes similar to the main analyses. Seventh, participants with cystatin C measurements available comprised a small proportion of otherwise eligible patients who had creatinine measurements in clinical cohorts and were likely not representative of these cohorts' overall study populations. Eighth, the association between eGFRdiff and longitudinal outcomes was not evaluated among hospitalized patients. Ninth, race and ethnicity data were not included in the analyses.

Conclusions

In the CKD-PC, 11% of outpatient participants and 35% of hospitalized patients had an eGFRcys that was at least 30% lower than eGFRcr. In the outpatient setting, presence of eGFRcys at least 30% lower than eGFRcr was associated with significantly higher rates of all-cause mortality, cardiovascular events, and kidney failure.

ARTICLE INFORMATION

Accepted for Publication: September 2, 2025.

Published Online: November 7, 2025. doi:10.1001/jama.2025.17578

Author Affiliations: Kidney Health Research Collaborative, University of California San Francisco and San Francisco Veterans Affairs Health Care System, San Francisco (Estrella, Chen, Shlipak); Optimal Aging Institute, New York University Grossman School of Medicine, New York (Ballew, Sang, Coresh); Division of Precision Medicine, Department of Medicine, New York University Grossman School of Medicine, New York (Grams, Surapaneni); Centre for Research in Epidemiology and Population Health (CESP), Paris-Saclay University, Inserm U1018, Versailles Saint-Quentin University, Clinical Epidemiology Team, Villejuif, France (Alencar de Pinho); School of Health and Social Studies, Dalarna University, Falun, Sweden (Ärnlöv); Department of Neurobiology, Care Sciences and Society, Family Medicine and Primary Care Unit, Karolinska Institutet, Huddinge, Sweden (Ärnlöv); Division of Clinical Epidemiology and Aging Research, German Cancer Research Center and Network Aging Research, Heidelberg University, Heidelberg, Germany (Brenner); Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Huddinge, Sweden (Carrero); Division of Nephrology, Department of Clinical Sciences, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden (Carrero); Division of Renal Electrolyte and Hypertension, Perelman School of Medicine, University of Pennsylvania, Philadelphia (Cohen); Departments of Medicine and Pathology and Laboratory Medicine, University of Vermont Larner College of Medicine, Burlington (Cushman); Department of Nephrology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands (Gansevoort); Framingham Heart Study, Framingham, Massachusetts (Hwang); Population Sciences Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland (Hwang); Division of Nephrology, Department of Medicine, Tufts Medical Center, Boston, Massachusetts (Inker, Levey); Nephrology Section, Veterans Affairs San Diego Health Care System, San Diego, California (Ix); Division of Nephrology-Hypertension, University of California San Diego, La Jolla (Ix); Department of Health Promotion Medicine, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan (Kabasawa); Division of Clinical Nephrology and Rheumatology, Kidney Research Center, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan (Kabasawa); Department of Public Health and Hygiene, Yamagata University, Yamagata, Japan (Konta); School of Cardiovascular & Metabolic Health, University of Glasgow, Glasgow, United Kingdom (Lees); Glasgow Renal and Transplant Unit, Queen Elizabeth University Hospital, Glasgow, United Kingdom (Lees); School of Public Health and Preventive Medicine and Department of Medicine, Monash University, Clayton, Victoria, Australia (Polkinghorne); Department of Nephrology, Monash Medical Centre, Monash Health, Clayton, Victoria, Australia (Polkinghorne); Department of Nephrology and Hypertension, University Medical Center Utrecht, Utrecht, the Netherlands (Vernooij); Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands (Vernooij); Centre for Kidney and Bladder Health, University College London, London, United Kingdom (Wheeler); Department of Experimental Medicine and Biotechnology, Postgraduate Institute of Medical Education and Research, Chandigarh, India (Yadav); Department of Nephrology and Hypertension, University Hospital Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany (Eckardt); Department of Nephrology and Medical Intensive Care, Charité-Universitätsmedizin Berlin, Berlin, Germany (Eckardt).

Author Contributions: Ms Sang and Dr Grams had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Estrella, Grams, Coresh, Carrero, Ix, Polkinghorne, Wheeler, Eckardt.
Acquisition, analysis, or interpretation of data: Estrella, Ballew, Sang, Grams, Coresh, Surapaneni, Alencar de Pinho, Ärnlöv, Brenner, Carrero, Chen, Cohen, Cushman, Gansevoort, Hwang, Inker, Kabasawa, Konta, Lees, Polkinghorne, Shlipak, Vernooij, Wheeler, Yadav, Levey.
Drafting of the manuscript: Estrella, Ballew, Inker, Shlipak, Eckardt.
Critical review of the manuscript for important intellectual content: Estrella, Ballew, Sang, Grams, Coresh, Surapaneni, Alencar de Pinho, Ärnlöv,

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Brenner, Carrero, Chen, Cohen, Cushman, Gansevoort, Hwang, Ix, Kabasawa, Konta, Lees, Polkinghorne, Shlipak, Vernooij, Wheeler, Yadav, Levey.
Statistical analysis: Sang, Surapaneni, Alencar de Pinho, Ärnlöv, Hwang, Inker, Lees.
Obtained funding: Grams, Coresh, Brenner, Cohen, Cushman, Lees, Wheeler.
Administrative, technical, or material support: Ballew, Coresh, Brenner, Carrero, Gansevoort, Polkinghorne, Vernooij, Yadav.
Supervision: Estrella, Ballew, Grams, Coresh, Gansevoort, Ix, Polkinghorne, Shlipak, Levey.

Conflict of Interest Disclosures: Dr Estrella reported receiving grants from Bayer; personal fees from Boehringer Ingelheim outside the submitted work; and being an executive board member of the National Kidney Foundation (NKF). Dr Grams reported receiving grants from the National Institutes of Health (NIH) and NKF during the conduct of the study; travel support from KDIGO (Kidney Disease: Improving Global Outcomes), American Society of Nephrology, and Kidney Research Institute (KRI); serving on the scientific advisory boards of KRI and NKF; and serving on the community advisory board of US Renal Data System (USRDS) outside the submitted work. Dr Alencar de Pinho reported receiving grants to her institution from Agence nationale de la recherche (ANR-IA-COH-2012/3731), Ministry of Higher Education and Research (2023-1322), GSK, Boehringer Ingelheim France, Novo Nordisk, Fresenius Medical Care, and Vifor France outside the submitted work. Dr Ärnlöv reported receiving personal fees from AstraZeneca, Boehringer Ingelheim, Astellas, and Novartis outside the submitted work. Dr Cohen reported receiving funding from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK; 5U01DK060984-25). Dr Kabasawa reported receiving Niigata Prefecture funding and grants from Japan Society for the Promotion of Science KAKENHI (17K15850, 23K09737, 23K07694) during the conduct of the study. Dr Konta reported receiving personal fees from Boehringer Ingelheim Japan, AstraZeneca Japan, Daiichi Sankyo, Pfizer, Chugai Pharmaceutical, Bayer, Mitsubishi Tanabe Pharma, Novartis, Mochida Pharmaceutical, Ono Pharmaceutical, MSD, Sanwa Kagaku Kenkyusho, Eisai, Kowa, Kyowa Kirin, and Fuji Yakuhin outside the submitted work. Dr Lees reported receiving personal fees from AstraZeneca and Boehringer Ingelheim outside the submitted work; and a Wellcome Trust Early-Career Award (301005/Z/23/Z). Dr Shlipak reported receiving grants paid to his institution from NIH during the conduct of the study; grants paid to his institution from NIH and Bayer; personal fees from Cardiovascular Health Study, Bayer, Boehringer Ingelheim, AstraZeneca, and Hagens Berman International Law Firm outside the submitted work; and serving as chair of the board for Northern California Institute for Research and Education. Dr Wheeler reported receiving personal fees from AstraZeneca, Astellas, Bayer, Boehringer Ingelheim, Eledon, Pathalys, ProKidney, Vifor, and Vertex outside the submitted work. Dr Levey reported receiving grants to his institution from NIH and royalties from UpToDate outside the submitted work. Dr Eckardt reported receiving grants from Evotec and Travere; and personal fees from Akebia, AstraZeneca, Boehringer Ingelheim, CSL Behring, GSK, Medice, Novartis, Novo Nordisk, Vera, Vicore, and Bayer outside the submitted work. No other disclosures were reported.

Funding/Support: The Chronic Kidney Disease Prognosis Consortium (CKD-PC) Data Coordinating Center is funded in part by a program grant from the NKF and NIDDK (R01DK100446). A variety of sources supported enrollment and data collection, including laboratory measurements and follow-up, in the collaborating cohorts of the CKD-PC. These funding sources include government agencies, such as national institutes of health and medical research councils as well as foundations and industry sponsors listed in eAppendix 3 in Supplement 1.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: The CKD-PC Investigators and Collaborators appear in Supplement 2.

Disclaimer: Some of the data reported here have been supplied by the USRDS. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the US government.

Meeting Presentation: This paper was presented at the Kidney Week Meeting of the American Society of Nephrology; November 7, 2025; Houston, TX.

Data Sharing Statement: See Supplement 3.

REFERENCES

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2024;105(4S):S117-S314. doi:10.1016/j.kint.2023.10.018

2. Chen DC, Potok OA, Rifkin D, Estrella MM. Advantages, limitations, and clinical considerations in using cystatin C to estimate GFR. *Kidney360*. 2022;3(10):1807-1814. doi:10.34067/KID.0003202022

3. Wang Y, Adingwupu OM, Shlipak MG, et al. Discordance between creatinine-based and cystatin C-based estimated GFR: interpretation according to performance compared to measured GFR. *Kidney Med*. 2023;5(10):100710. doi:10.1016/j.xkme.2023.100710

4. Fu EL, Levey AS, Coresh J, et al. Accuracy of GFR estimating equations in patients with discordances between creatinine and cystatin C-based estimations. *J Am Soc Nephrol*. 2023;34(7):1241-1251. doi:10.1681/ASN.0000000000000128

5. Chen DC, Shlipak MG, Scherzer R, et al. Association of intraindividual difference in estimated glomerular filtration rate by creatinine vs cystatin C and end-stage kidney disease and mortality. *JAMA Netw Open*. 2022;5(2):e2148940. doi:10.1001/jamanetworkopen.2021.48940

6. Chen DC, Shlipak MG, Scherzer R, et al. Association of intra-individual differences in estimated GFR by creatinine versus cystatin C with incident heart failure. *Am J Kidney Dis*. 2022;80(6):762-772.e1. doi:10.1053/j.ajkd.2022.05.011

7. Potok OA, Ix JH, Shlipak MG, et al. The difference between cystatin C- and creatinine-based estimated GFR and associations with frailty and adverse outcomes: a cohort analysis of the Systolic Blood Pressure Intervention Trial (SPRINT). *Am J Kidney Dis*. 2020;76(6):765-774. doi:10.1053/j.ajkd.2020.05.017

8. Carrero JJ, Fu EL, Sang Y, et al. Discordances between creatinine- and cystatin C-based estimated GFR and adverse clinical outcomes in routine clinical practice. *Am J Kidney Dis*. 2023;82(5):534-542. doi:10.1053/j.ajkd.2023.04.002

9. Inker LA, Eckfeldt J, Levey AS, et al. Expressing the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) cystatin C equations for estimating GFR with standardized serum cystatin C values. *Am J Kidney Dis*. 2011;58(4):682-684. doi:10.1053/j.ajkd.2011.05.019

10. Grubb A, Blirup-Jensen S, Lindström V, Schmidt C, Althaus H, Zegers I; IFCC Working Group on Standardisation of Cystatin C (WG-SCC). First certified reference material for cystatin C in human serum ERM-DA471/IFCC. *Clin Chem Lab Med*. 2010;48(11):1619-1621. doi:10.1515/CCLM.2010.318

11. Inker LA, Eneanya ND, Coresh J, et al; Chronic Kidney Disease Epidemiology Collaboration. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med*. 2021;385(19):1737-1749. doi:10.1056/NEJMoa2102953

12. Inker LA, Schmid CH, Tighiouart H, et al; CKD-EPI Investigators. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. 2012;367(1):20-29. doi:10.1056/NEJMoa1114248

13. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. *Am J Kidney Dis*. 2022;79(2):268-288.e1. doi:10.1053/j.ajkd.2021.08.003

14. Genzen JR, Souers RJ, Pearson LN, et al. Reported awareness and adoption of 2021 estimated glomerular filtration rate equations among US clinical laboratories, March 2022. *JAMA*. 2022;328(20):2060-2062. doi:10.1001/jama.2022.15404

15. Chen DC, Lu K, Scherzer R, et al. Cystatin C- and creatinine-based estimated GFR differences: prevalence and predictors in the UK Biobank. *Kidney Med*. 2024;6(4):100796. doi:10.1016/j.xkme.2024.100796

16. Potok OA, Ix JH, Shlipak MG, et al. Cystatin C- and creatinine-based glomerular filtration rate estimation differences and muscle quantity and functional status in older adults: the Health, Aging, and Body Composition study. *Kidney Med*. 2022;4(3):100416. doi:10.1016/j.xkme.2022.100416

17. Farrington DK, Surapaneni A, Matsushita K, Seegmiller JC, Coresh J, Grams ME. Discrepancies between cystatin C-based and creatinine-based eGFR. *Clin J Am Soc Nephrol*. 2023;18(9):1143-1152. doi:10.2215/CJN.0000000000000217

18. United States Renal Data System. *2024 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States*. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2024.

19. Kumar V, Yadav AK, Gang S, et al. Indian chronic kidney disease study: design and methods.

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025

Nephrology (Carlton). 2017;22(4):273-278. doi:10.1111/nep.12789

20. Stengel B, Combe C, Jacquelinet C, et al. The French Chronic Kidney Disease-Renal Epidemiology and Information Network (CKD-REIN) cohort study. *Nephrol Dial Transplant*. 2014;29(8):1500-1507. doi:10.1093/ndt/gft388

21. Nerpin E, Ingelsson E, Risérus U, et al. The combined contribution of albuminuria and glomerular filtration rate to the prediction of cardiovascular mortality in elderly men. *Nephrol Dial Transplant*. 2011;26(9):2820-2827. doi:10.1093/ndt/gfq848

22. Gasparini A, Evans M, Coresh J, et al. Prevalence and recognition of chronic kidney disease in Stockholm healthcare. *Nephrol Dial Transplant*. 2016;31(12):2086-2094. doi:10.1093/ndt/gfw354

23. Konta T, Hao Z, Abiko H, et al. Prevalence and risk factor analysis of microalbuminuria in Japanese general population: the Takahata study. *Kidney Int*. 2006;70(4):751-756. doi:10.1038/sj.ki.5001504

24. Landray MJ, Thambyrajah J, McGlynn FJ, et al. Epidemiological evaluation of known and suspected cardiovascular risk factors in chronic renal impairment. *Am J Kidney Dis*. 2001;38(3):537-546. doi:10.1053/ajkd.2001.26850

25. Klahr S, Levey AS, Beck GJ, et al; Modification of Diet in Renal Disease Study Group. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. *N Engl J Med*. 1994;330(13):877-884. doi:10.1056/NEJM199403313301301

26. Zhang QL, Koenig W, Raum E, Stegmaier C, Brenner H, Rothenbacher D. Epidemiology of chronic kidney disease: results from a population of older adults in Germany. *Prev Med*. 2009;48(2):122-127. doi:10.1016/j.ypmed.2008.10.026

27. Howard VJ, Cushman M, Pulley L, et al. The Reasons for Geographic and Racial Differences in Stroke study: objectives and design. *Neuroepidemiology*. 2005;25(3):135-143. doi:10.1159/000086678

28. Titze S, Schmid M, Köttgen A, et al; GCKD study investigators. Disease burden and risk profile in referred patients with moderate chronic kidney disease: composition of the German Chronic Kidney Disease (GCKD) cohort. *Nephrol Dial Transplant*. 2015;30(3):441-451. doi:10.1093/ndt/gfu294

29. Parikh NI, Hwang SJ, Larson MG, Levy D, Fox CS. Chronic kidney disease as a predictor of cardiovascular disease (from the Framingham Heart Study). *Am J Cardiol*. 2008;102(1):47-53. doi:10.1016/j.amjcard.2008.02.095

30. Denker M, Boyle S, Anderson AH, et al; Chronic Renal Insufficiency Cohort Study Investigators. Chronic Renal Insufficiency Cohort Study (CRIC): overview and summary of selected findings. *Clin J Am Soc Nephrol*. 2015;10(11):2073-2083. doi:10.2215/CJN.04260415

31. US Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. Accessed January 19, 2017. https://wwwn.cdc.gov/nchs/nhanes/Default.aspx

32. Matsushita K, Selvin E, Bash LD, Franceschini N, Astor BC, Coresh J. Change in estimated GFR associates with coronary heart disease and mortality. *J Am Soc Nephrol*. 2009;20(12):2617-2624. doi:10.1681/ASN.2009010025

33. Shlipak MG, Katz R, Kestenbaum B, et al. Rate of kidney function decline in older adults: a comparison using creatinine and cystatin C. *Am J Nephrol*. 2009;30(3):171-178. doi:10.1159/000212381

34. van Zuilen AD, Bots ML, Dulger A, et al. Multifactorial intervention with nurse practitioners does not change cardiovascular outcomes in patients with chronic kidney disease. *Kidney Int*. 2012;82(6):710-717. doi:10.1038/ki.2012.137

35. Hillege HL, Fidler V, Diercks GF, et al; Prevention of Renal and Vascular End Stage Disease (PREVEND) Study Group. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation*. 2002;106(14):1777-1782. doi:10.1161/01.CIR.0000031732.78052.81

36. Bycroft C, Freeman C, Petkova D, et al. The UK Biobank resource with deep phenotyping and genomic data. *Nature*. 2018;562(7726):203-209. doi:10.1038/s41586-018-0579-z

37. Wright JT Jr, Bakris G, Greene T, et al; African American Study of Kidney Disease and Hypertension Study Group. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA*. 2002;288(19):2421-2431. doi:10.1001/jama.288.19.2421

38. Bui AL, Katz R, Kestenbaum B, et al. Cystatin C and carotid intima-media thickness in asymptomatic adults: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Kidney Dis*. 2009;53(3):389-398. doi:10.1053/j.ajkd.2008.06.025

39. White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) study GFR estimating equations: the AusDiab (Australian Diabetes, Obesity and Lifestyle) study. *Am J Kidney Dis*. 2010;55(4):660-670. doi:10.1053/j.ajkd.2009.12.011

40. Kabasawa K, Tanaka J, Nakamura K, et al. Study design and baseline profiles of participants in the Uonuma CKD cohort study in Niigata, Japan. *J Epidemiol*. 2020;30(4):170-176. doi:10.2188/jea.JE20180220

41. Potok OA, Katz R, Bansal N, et al. The difference between cystatin C- and creatinine-based estimated GFR and incident frailty: an analysis of the Cardiovascular Health Study (CHS). *Am J Kidney Dis*. 2020;76(6):896-898. doi:10.1053/j.ajkd.2020.05.018

42. Liu L, Chang DY, Lewandrowski KB, Dighe AS. Discrepancy between estimated glomerular filtration rate by creatinine versus cystatin C in different patient care settings. *Clin Biochem*. 2024;131-132:110801. doi:10.1016/j.clinbiochem.2024.110801

43. Chen DC, Lees JS, Lu K, et al. Differential associations of cystatin C versus creatinine-based kidney function with risks of cardiovascular event and mortality among South Asian individuals in the UK Biobank. *J Am Heart Assoc*. 2023;12(3):e027079. doi:10.1161/JAHA.122.027079

44. Shlipak MG, Sarnak MJ, Katz R, et al. Cystatin C and the risk of death and cardiovascular events among elderly persons. *N Engl J Med*. 2005;352(20):2049-2060. doi:10.1056/NEJMoa043161

45. Shlipak MG, Matsushita K, Ärnlöv J, et al; CKD Prognosis Consortium. Cystatin C versus creatinine in determining risk based on kidney function. *N Engl J Med*. 2013;369(10):932-943. doi:10.1056/NEJMoa1214234

46. Grams ME, Coresh J, Matsushita K, et al; Writing Group for the CKD Prognosis Consortium. Estimated glomerular filtration rate, albuminuria, and adverse outcomes: an individual-participant data meta-analysis. *JAMA*. 2023;330(13):1266-1277. doi:10.1001/jama.2023.17002

© 2025 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Downloaded from jamanetwork.com by Universidad Nacional Autonoma de Mexico (UNAM) user on 11/14/2025